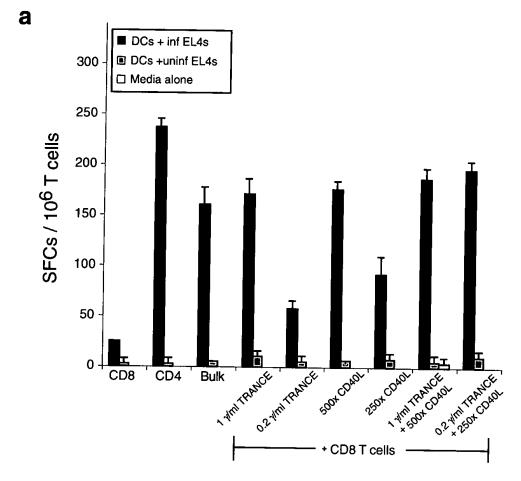
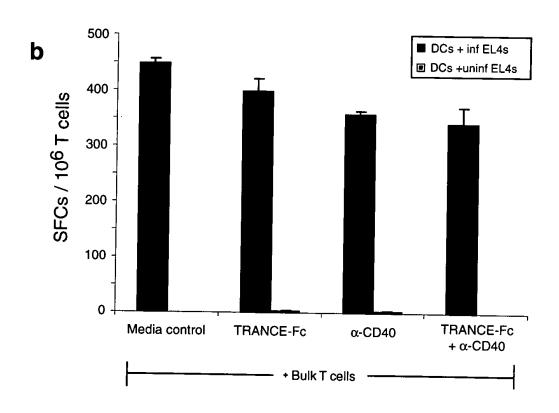
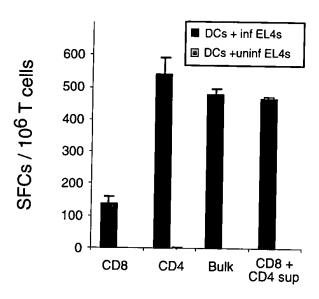


TOSTUSEL TETPO

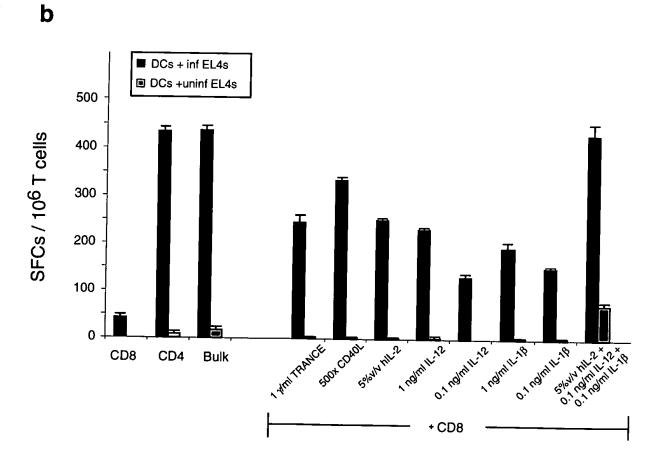




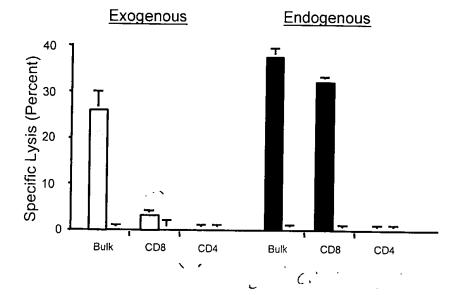


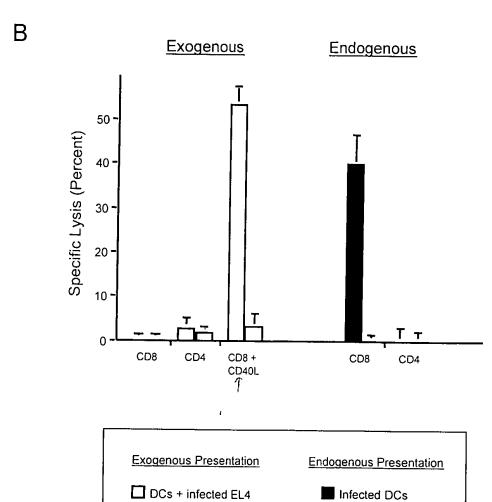






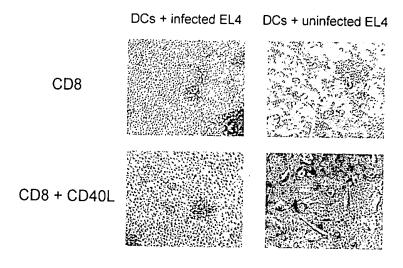
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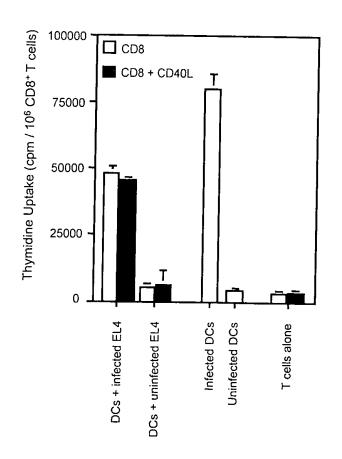


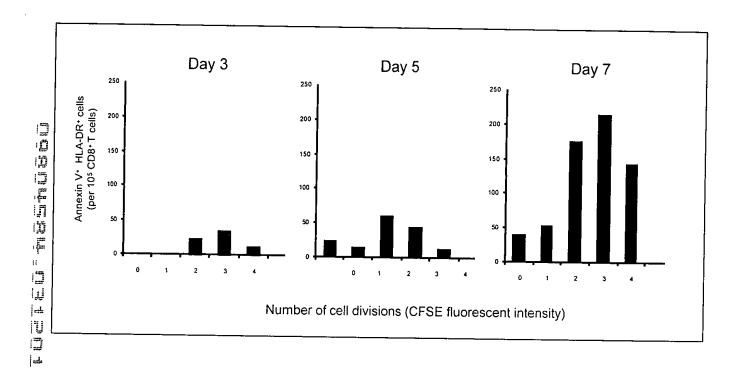
DCs + uninfected EL4

Uninfected DCs

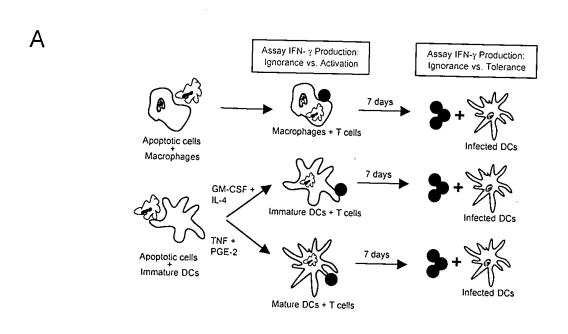


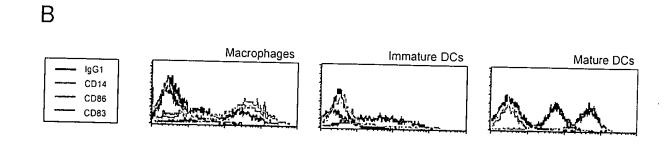
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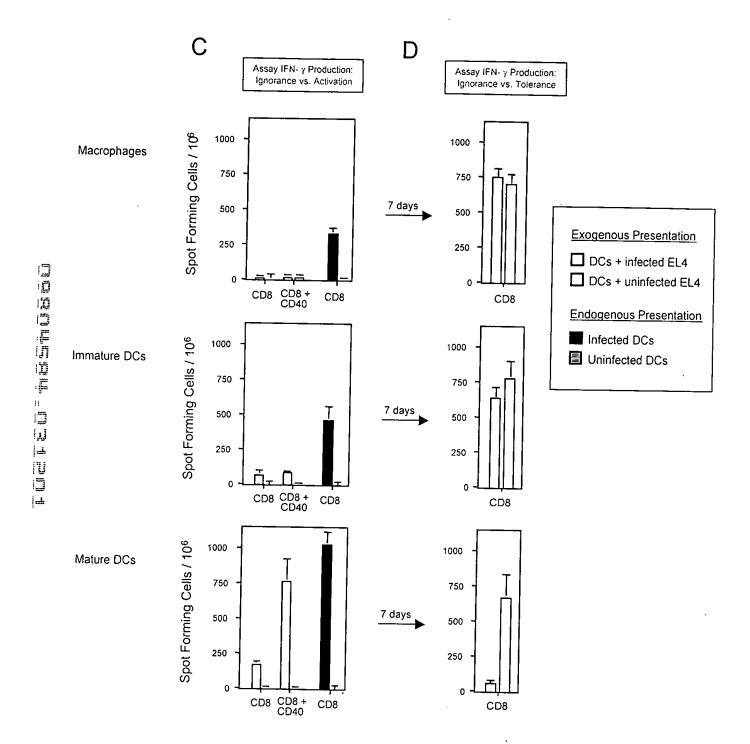


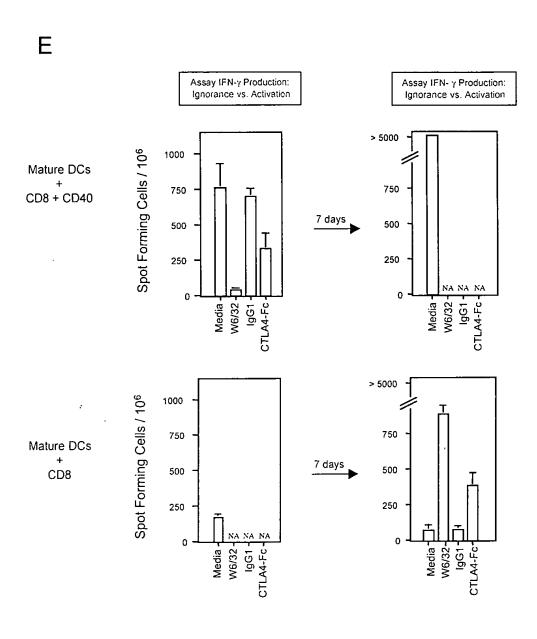




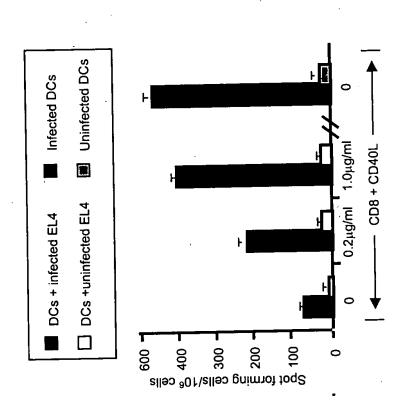








CD4 helper cells 'license' the DC to cross-prime via CD40 ligation

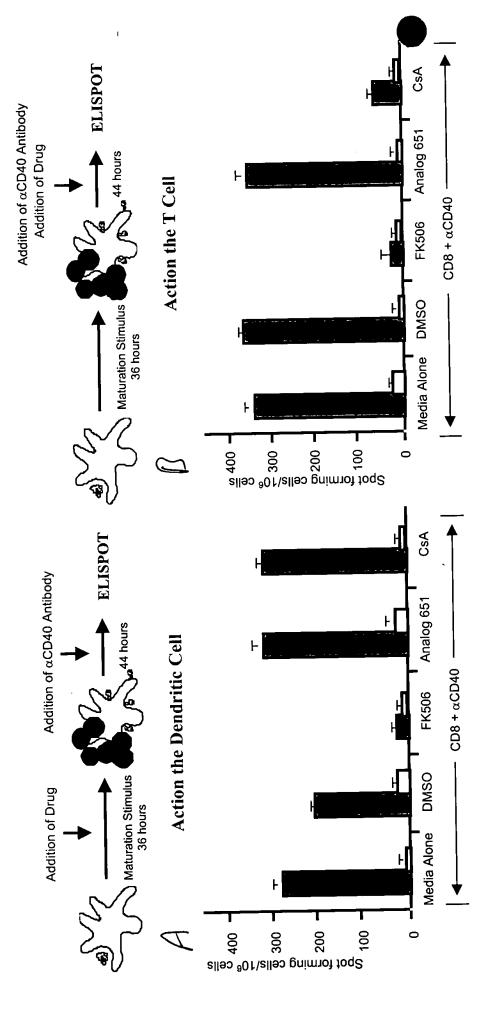


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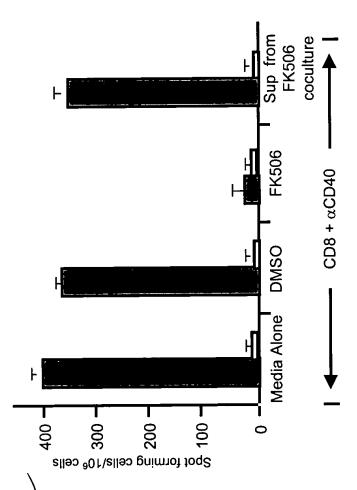
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Collination Collination

FK506, but not CsA inhibits cross-priming by affecting the DC



No residual FK506 remains in coculture



Cocultures were established as previously described with the addition of FK506 during the 36 hour DC-Apoptotic cell coculture. DCs were collected, washed, counted and plated in wells containing purified CD8+ T cells with αCD40 antibody with the addition of supernatant from the FK506 DC-Apoptotic cell coculture to untreated DCs. No residual FK506 remained in the coculture to inhibit T cell activation. Red bars, DCs + infected EL4 cells; White bars, DCs + uninfected EL4 cells.

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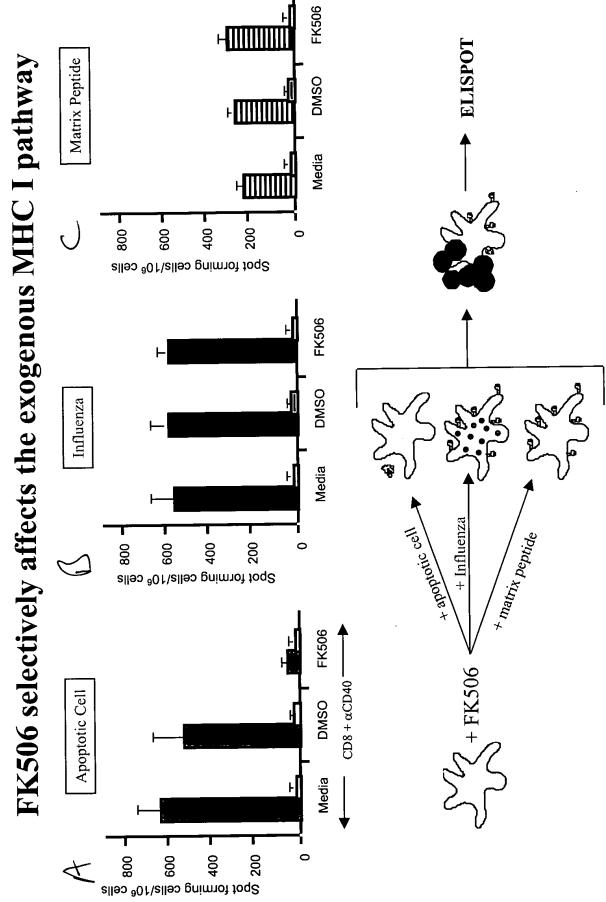
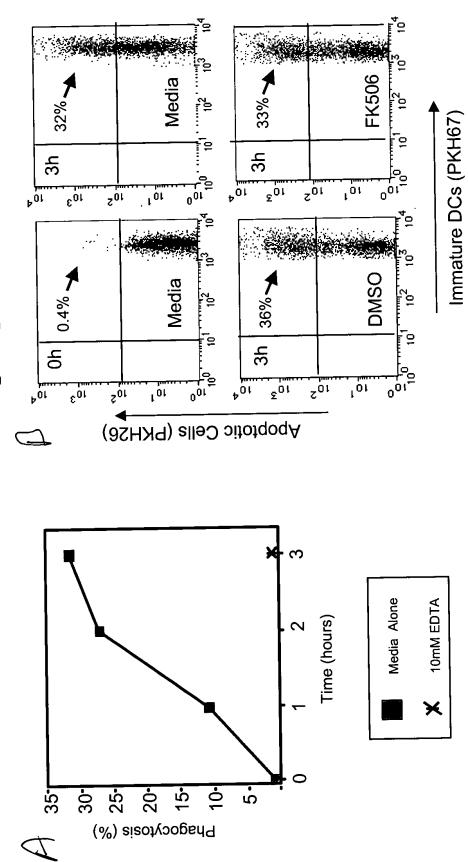


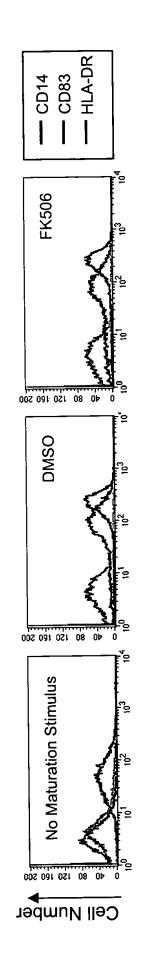
FIG 11 A-B

FK506 does not inhibit phagocytosis



cocultured with the apoptotic cells. Cocultures were then analyzed by FACS, gating on dendritic cells. Double positive cells were scored as a measure of percent phagocytosis. FK506 does not Day 6 immature DCs were treated with 0.5µM FK506 for 24 hours, dyed with PKH67 and then EL4 cells were dyed with PKH26, UVB irradiated and allowed to undergo apoptosis for 8 hours. inhibit antigen capture.

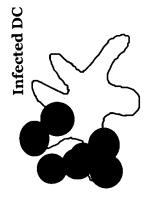
FK506 does not inhibit Dendritic Cell maturation



Cultures were established as previously described with the addition of 0.5 μ M FK506 during the 36 hour DC-Apoptotic cell coculture. DCs were collected, washed and stained for HLA-DR. HLA-DR+ DCs were then gated on to exclude apoptotic debris and analyzed by FACS for their CD14, CD83 and HLA-DR expression. FK506 does not act to inhibit cross-priming by affecting DC maturation.

Ple IID

FK506 does not inhibit generation of MHC I / peptide complex



DMSO DCs + infected EL4

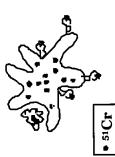
Media DCs + infected EL4

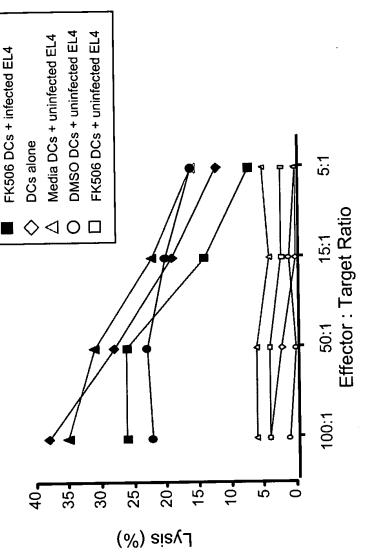
Peptide pulsed DCs

Influenza Specific CTLs used as effector cells

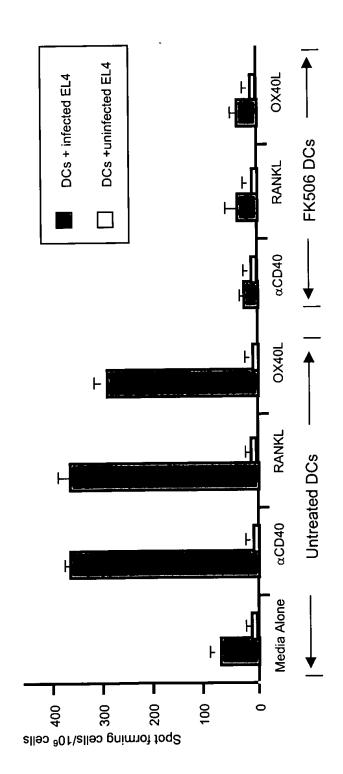


DCs cross-presenting apoptotic cells used as targets





FK506 acts to inhibit cross-priming by blocking signaling of TNF superfamily members



FK506 treated DCs block signaling of CD40, RANK and OX40 in the Cocultures were established as previously described +/- FK506 treatment. DCs were collected, counted and plated in wells containing purified CD8⁺ T cells ELISPOT assay was performed and spot forming cells/106 cells are reported. (Kamiya Biomedical), or human recombinant OX40L (Alexis Biochemicals). with 1µg/mL \alpha CD40 antibody (Mabtech), human recombinant RANKL exogenous pathway.

Assaying for Tolerance vs. Ignorance

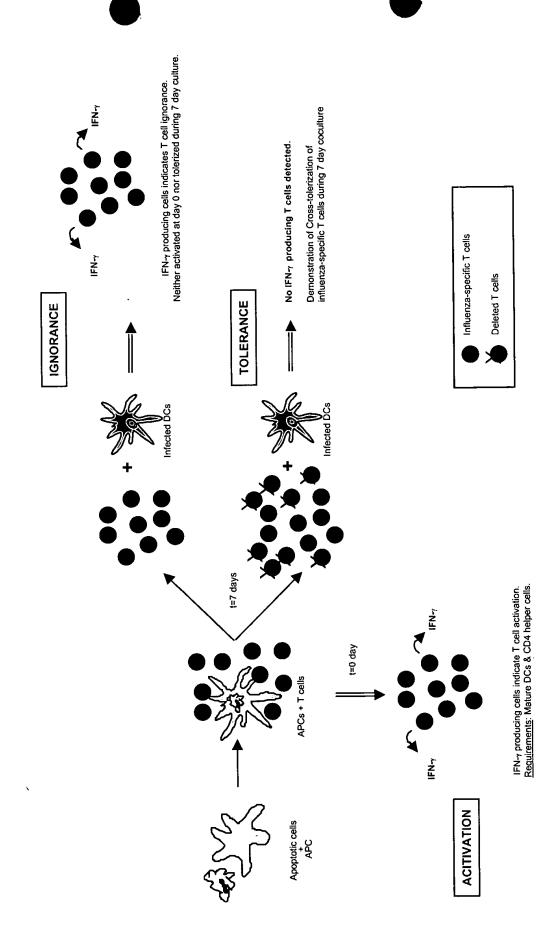


FIG 17

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FK506 cross-tolerizes antigen specific CD8+ T cells

